REMARKS

Claims 1-15, 17-21, 23-27, and 29-33 are pending in this application. Claims 16, 22 and 28 previously were canceled.

Claims 1, 7, 11, 23, 29 and 30 currently have been amended. Claims 21, 26 and 32 have been canceled herein. Claims 34-39 are new.

Claim 1 has been amended to recite "... effective in establishing in vivo a pH..."

Claims 7, 11, 23 and 29 have been amended to overcome informalities.

The support for newly added claims 34, 35 and 36 can be found for example in paragraph [0084] which states: "In other embodiments, the monomeric units of either the biodegradable polymer or the oligomers, or both may be different than the monomers of the acidity regulating component."

Claims 37-39 find support in the instant specification in Examples 1-4.

The current amendments or cancellations have been made without disclaimer, prejudice or estoppel and solely to expedite prosecution. Applicants do not acquiesce to the propriety of any of the Office's issued rejections and may pursue canceled, excised or originally claimed subject matter in one or more future applications.

Claim Objections

Claims 7 and 11 are objected to because of informalities. Applicants currently have amended claims 7 and 11 to show the punctuation mark of a period.

Claim 21 was objected to as being an improper dependent claim. Claim 21 has been canceled herein without disclaimer or prejudice. Thus, Applicants submit the objection has been obviated.

Claim 23 was objected to as being an improper dependent claim. Claim 23 currently has been amended to recite "… from a second biodegradable polymer." In view of this amendment, Applicants submit the objection has been obviated.

Claim 29 was objected to as being an improper dependent claim. Claim 29 currently has been amended to depend on claim 1. In view of this amendment, Applicants submit the objection has been obviated.

Claim 32 was objected to as being an improper dependent claim. Claim 32 has been canceled herein without disclaimer or prejudice. Thus, this objection has been obviated.

35 USC § 102 Rejections

Claims 1-15. 17-21, 23-27 and 29-33 are rejected under 35 USC § 102(b) as anticipated by U.S. 6,506,399 ('399 patent), or Donovan et al. 6,312,708 ('708 patent).

Applicants respectfully traverse.

The law is clear that in order to anticipate a claim, a single source must contain all of the elements of the claim. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81, 90 (Fed. Cir. 1986); *Atlas Powder Co. v. E.I. du Pont De Nemours & Co.*, 224 USPQ 409, 411 (Fed. Cir. 1984). Moreover, the single source must disclose all of the claimed elements "arranged as in the claim." *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989); *Connell v. Sears Roebuck & Co.*, 220 USPQ 193, 198 (Fed. Cir. 1983). Finally, the law requires identity between the claimed invention and the prior art disclosure. *Kalman v. Kimberly-Clark Corp.*, 218 USPQ2d 781, 789 (Fed. Cir. 1983, cert denied, 465 U.S. 1026 (1984)).

Applicants submit that the current limitation in claim 1 "an acidity regulating component effective in ~~for~~ establishing in vivo a pH in the vicinity of the neurotoxin component associated with the implant of less than about 7" carries patentable weight and must be considered. The presently claimed invention achieves the indicated pH

level(s) but the Office has not put forth any evidence that the cited reference achieves the same results arising from the claimed elements and limitations. Even accepting *arguendo*, the Office's assertion that degradation of polymers lowers pH, one cannot assume that the lowering of pH is to the level required by present claim 1 without evidence put forth by the Office indicating this.

Moreover, relying on degradation from a polymer carrier to effectively regulate pH is a concept which runs counter to the accepted knowledge in the field. Acidic and basic excipients had been incorporated into biodegradable polymers such as poly(lactic-co-glycolic acid) (PLGA), poly(ortho ester) and other polyester polymers to catalyze polymer degradation. Unfortunately, these excipients tended to diffuse away from polymeric implants and cause tolerability issues. (*See* paragraph [0041] of instant specification). If PLGA degradation could simply produce a regulated microenvironment why would there be a need to provide acidic and basic excipient catalysts? The presently claimed invention achieved this and other objectives by providing acidic regulating components comprising monomers and oligomers.

The monomers and oligomers of acidity regulating component in accordance with the presently claimed invention typically degrade at a relatively faster rate than the polymer or generate acid functionalities at a faster rate. Thus, they are effective in maintaining an acidic environment or microenvironment of a neurotoxin implant. (*See* paragraph [0084] of the instant specification.)

Further, the Federal Circuit clarified in a recently decided case, *Net Moneyin Inc. v. Verisign, Inc.*, Fed. Cir. No. 2007-1565 (October 20, 2008):

> The meaning of the expression "arranged as in the claim" is readily understood in relation to claims drawn to things such as ingredients mixed in some claimed order. In such instances, a reference that discloses all of the claimed ingredients, but not in the order claimed, would not anticipate, because the reference would be missing any disclosure of the limitations of the claimed invention "arranged as in the claim." But the "arranged as in the claim" requirement is not limited to such a narrow set of "order of limitations" claims. Rather, out precedent informs that the "arranged as in the claim" requirement applies to all claims and refers to the need for an

> anticipatory reference to show all of the limitations of the claims arranged or combined in the same way recited in the claims, not merely in a particular order. The test is thus more accurately understood to mean "arranged or combined in the same way as in the claim." (Emphasis supplied).

In the present case, neither of the Office's cited references shows all of the elements of Applicants' presently claimed invention. Moreover, the references do not show the claimed elements, biodegradable polymer with monomers and oligomers in the same way as recited in the claims. Donovan supplies polymers but not monomers and oligomers initially furnished in addition to biodegradable polymers.

Because Donovan does not identically teach each and every element of the currently amended claims, it does not anticipate the presently claimed invention. Applicants respectfully request withdrawal of the rejection under 35 USC § 102(b) as being anticipated by Donovan et al. (US 6,506,399) or Donovan et al. (US 6,312,708).

Alternatively, Applicants further note that newly added claims 34-36 recite "… wherein the acidity regulating component comprises a monomer and an oligomer derived from a different biodegradable polymer.

Neither the '399 patent nor the '708 patent identically teach an acidity regulating component comprising a monomer and an oligomer derived from a different biodegradable polymer.

Thus, the following assertion by the Office cannot be true: "Donovan et al. disclose of the same biodegradable polymers as claimed, e.g., PLGA. (See claims and paragraph 84 of '399). Furthermore, the PLGA polymer disclosed by Donovan inherently comprises oligomers and monomers of PLGA, as each are building blocks of the polymer molecule. Furthermore, oligomers and monomers of PLGA will be spontaneously generated in vivo as the polymer breaks down" (Instant Office action, Page 5, ¶3).

The instant claims specify that the acidity regulating component is composed of monomers and oligomers of a different biodegradable polymer from the separate and

distinct biodegradable polymer component of the presently claimed invention. Thus, the cited references cannot inherently comprise oligomers and monomers of the same polymer such as PLGA. Moreover, the oligomers and monomers derived from a different biodegradable polymer means that the spontaneous generation by polymer breakdown is not primarily responsible for the resulting acidity regulating effect.

In view of the foregoing, Applicants submit that the presently newly added claims 34-36 are novel over Donovan et al. (US 6,506,399) or Donovan et al. (US 6,312,708).

Further alternatively, Applicants submit that the newly added claims which recite the weight percentages of the monomer and oligomer component as compared the biodegradable polymer component and/or recite the ratio of monomers and oligomers, are not anticipated by the cited references. Neither the '399 nor the '708 patent teaches the weigh percentages or the monomer to oligomer ratios.

In view of the foregoing, Applicants submit that the presently newly added claims 37-39 are novel over Donovan et al. (US 6,506,399) or Donovan et al. (US 6,312,708).

In view of the foregoing, Applicants respectfully request withdrawal of the rejection under 35 USC § 102(b) as being anticipated by Donovan et al. (US 6,506,399) or Donovan et al. (US 6,312,708). Favorable action is solicited.

35 USC § 103 Rejections

Claims 1-15, 17-21, 23-27 and 29-33 are rejected under 35 USC § 103(a) as being unpatentable over Donovan et al in view of Schwendeman et al.

Applicants respectfully traverse.

To maintain a proper rejection under 35 USC § 103, the Examiner must meet four conditions to establish a *prima facie* case of obviousness. First, the Examiner must show that the prior art suggested to those of ordinary skill in the art that they should make the claimed composition or device or carry out the claimed process. Second, the Examiner must show that the prior art would have provided one of ordinary skill in the

art with a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be adequately founded in the prior art and not in an applicant's disclosure. Third, the prior art must teach or suggest all the claim limitations. *In re Vaeck,* 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991). Fourth, if an obviousness rejection is based on some combination of prior art references, the Examiner must show a suggestion, teaching, or motivation to combine the prior art references ("the TSM test"). *In re Dembiczak,* 50 U.S.P.Q.2d 1614, 1617 (Fed. Cir. 1999). Following *KSR Int'l Co. v. Teleflex, Inc.*, this fourth prong of the *prima facie* obviousness analysis must not be applied in a rigid or formulaic way such that it becomes inconsistent with the more flexible approach of *Graham v. John Deere*, 383 U.S. 1, 17-18 (1966); 127 S. Ct. 1727 (2007). It must still be applied, however, as the TSM test captures the important insight that "a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *Id.* at 1741 (citing *United States v. Adams*, 383 U.S. 39, 50-52 (1966)).

Schwendeman et al. teaches away from using an acidity regulating component to create a microenvironment with a lowered pH.

With neurotoxins generally, the goal is to maintain a pH value of less than about 7. This environment effectively stabilizes the neurotoxin. When the pH is less than about 7, a neurotoxin such as botulinum toxin may be maintained for prolonged periods of time, perhaps even for the life of the implant. (Paragraph [0079] of the instant specification).

Schwendeman et al. disclosed methods which guard against degradation by acids. Thus in paragraph [0006] it states:

> In accordance with the present invention, it has been discovered that, in many instances, the acids that are produced during biodegradation of PLGA can induce an irreversible inactivation or instability of biologically active agents, such as for example proteins, drugs, oligonucleotides and

> vaccine agents. It has also been determined that the addition of certain antacids, such as for example $MgOH_2$, to the system will not significantly reduce the acid-induced instability of the biologically active unless the polymer is prepared in a manner which results in the formation of an interconnected network of pores within the polymer.

The whole aim of Schwendeman et al. was to prevent acid degradation of a polymer such as PLGA. Thus, in order to arrive at the presently claimed invention, one of ordinary skill in the art would have to ignore this overarching goal of Schwendeman et al. Schwendeman et al. directs a skilled artisan to go one way: find ways to reduce or prevent acid-induced instability. To get to the presently claimed invention, the skilled artisan would have to go the other way: find ways to lower the pH to promote neurotoxin stability. Proceeding contrary to the accepted wisdom of the prior art is strong evidence of nonobviousness. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303, 213 (Fed. Cir. 1983); *In re Hedges*, 783 F.2d 1038, 228 USPQ 685, 687 (Fed. Cir. 1986).

The Office's assertions appear to entirely rest on the statement of Schwendeman et al. in paragraph [0084]: "The presence of monomers or oligomers can also produce acidic microclimate even before polymer degradation occurs." However, simply plucking this sentence out of the entire disclosure of Schwendeman et al. is not, Applicants respectfully submit, a proper way of finding the necessary rationale for combining Schwendeman et al. with any of the other cited references. In view of the teaching directing one of ordinary skill in the art against using the reference to achieve a stabilizing acidic environment, Applicants submit that one of ordinary skill in the art would not have combined Schwendeman et al. with Donovan et al. It is impermissible within the framework of 35 USC § 103 to pick and choose from any one reference only so much of it as will support a given position to the exclusion of other parts necessary to full appreciation of what such reference fairly suggests to one skilled in the art. *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.*, 796 F.2d 443, 230 USPQ 416 (Fed. Cir. 1986).

Alternatively, the cited references, even when combined do not teach or suggest the element in new claims 34-36: "… wherein the acidity regulating component comprises a monomer and an oligomer derived from ~~the same~~ a different biodegradable polymer." The cite references, even when combined do not teach or suggest the element in new claims 37-38 which are the weight percentages of the monomer and oligomer component as compared the biodegradable polymer component and/or the ratio of monomers and oligomers.

In view of the foregoing, Applicants respectfully request the Office to withdraw the rejection of claims 1-15, 17-21, 23-27 and 29-33 und 35 USC § 103(a). Favorable action is solicited.

CONCLUSION

Applicant respectfully requests that a timely Notice of Allowance be issued in this case. The Commissioner is authorized to charge any fee which may be required in connection with this Amendment to deposit account No. 50-3207.

Respectfully submitted,

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